

WHAT IS CLAIMED IS:

- 1 1. A method for assessment of the intra-amniotic environment,
2 comprising (A) obtaining a vaginal sample from a subject, and
3 (B) subjecting the sample to analysis, to determine presence or absence in
4 the sample of a plurality of biomarkers that is indicative of status of the
5 intra-amniotic environment, such that results from the assessment of the
6 vaginal sample informs a diagnostic or prognostic determination in relation
7 to the subject.
- 8 2. The method as claimed in claim 1, wherein (A) and (B) are
9 repeated at least at a second time.
- 10 3. The method as claimed in claim 1, wherein the biomarkers are
11 indicative of rupture of the fetal membrane.
- 12 4. The method as claimed in claim 1, wherein the biomarkers are
13 indicative of intra-amniotic infection.
- 14 5. The method as claimed in claim 1, wherein the biomarkers are
15 indicative of intra-amniotic inflammation.
- 16 6. The method as claimed in claim 1, wherein the biomarkers are
17 indicative of fetal lung maturation.
- 18 7. The method as claimed in claim 1, wherein the biomarkers are
19 selected from the group consisting of alpha-fetoprotein, fetal fibronectin,
20 insulin-like growth factor binding protein-1, prolactin and human placental
21 lactogen, and fragments thereof.
- 22 8. The method as claimed in claim 1, wherein the biomarkers are
23 selected from the group consisting of beta-2-microglobulin and cystatin-C,

24 and fragments thereof.

25 9. The method as claimed in claim 1, wherein the plurality of
26 biomarkers is subjected to pattern recognition analysis.

27 10. The method as claimed in claim 1, wherein the method is an
28 ELISA.

29 11. The method as claimed in claim 1, wherein the method
30 comprises mass spectrometric analysis effected via SELDI.

31 12. The method as claimed in claim 11, wherein the method
32 comprises applying the vaginal sample to a biochip comprising at least
33 one absorbent selected from the group consisting of a hydrophobic
34 adsorbent and a cation exchange adsorbent.

35 13. The method as claimed in claim 11, the mass spectrometric
36 analysis comprises subjecting mass-spectrometry peak data obtained for
37 the vaginal sample to software analysis comprised of an algorithm for
38 analyzing data extracted from a spectrum.

39 14. The method as claimed in claim 13, wherein the algorithm
40 implements a pattern-recognition analysis that is keyed to data relating to
41 at least one of the biomarkers.

42 15. The method as claimed in claim 1, wherein a first vaginal
43 sample is collected early during a pregnancy and contributes to a baseline
44 against which subsequent vaginal samples are compared.

45 16. The method as claimed in claim 15, wherein the
46 determination includes a recommendation for treatment.

47 17. The method as claimed in claim 16, further comprising

48 monitoring the treatment by assaying at least one vaginal sample during
49 treatment, to determine the presence or absence in the vaginal sample of
50 biomarkers that are indicative of status of the intra-amniotic environment.

51 18. The method as claimed in claim 16, wherein the
52 determination includes a recommendation of treatment that comprises
53 antibiotic treatment, tocolytic treatment, anti-inflammatory treatment, or
54 antioxidant treatment.

55 19. The method as claimed in claim 16, wherein the
56 determination includes a recommendation of treatment that comprises
57 inducing labor.

58 20. The method as claimed in claim 16, wherein the
59 determination includes a recommendation of treatment that comprises a
60 cesarean section.

61 21. A method for assessment of the intra-amniotic environment,
62 comprising (A) obtaining a vaginal sample from a subject, (B) subjecting
63 the sample to analysis, to determine the presence or absence in the
64 sample of one or more oxidized or carbonylated peptides that are
65 indicative of status of the intra-amniotic environment, such that results
66 from the assessment of the vaginal sample informs a diagnostic or
67 prognostic determination in relation to the subject.

68 22. The method as claimed in claim 21, wherein the vaginal
69 sample is treated with dinitrophenol which is incorporated into the
70 oxidized or carbonylated peptide.

71 23. The method as claimed in claim 21, wherein the method is
72 an ELISA.

73 24. The method as claimed in claim 21, wherein the method
74 comprises mass spectrometric analysis effected via SELDI.

75 25. The method as claimed in claim 21, wherein the method
76 comprises applying the vaginal sample to a biochip comprising at least
77 one absorbent selected from the group consisting of a hydrophobic
78 adsorbent and a cation exchange adsorbent.

79 26. The method as claimed in claim 24, wherein the mass
80 spectrometric analysis comprises subjecting mass-spectrometry peak data
81 obtained for the vaginal sample to software analysis comprised of an
82 algorithm for analyzing data extracted from a spectrum.

83 27. The method as claimed in claim 26, wherein the algorithm
84 implements a pattern-recognition analysis that is keyed to data relating to
85 a plurality of oxidized or carbonylated peptides.

86 28. The method as claimed in claim 21, wherein a plurality of
87 oxidized or carbonylated peptides is subjected to pattern recognition
88 analysis.

89 29. The method as claimed in claim 21, wherein a first vaginal
90 sample is collected early during a pregnancy and contributes to a baseline
91 against which subsequent vaginal samples are compared.

92 30. The method as claimed in claim 21, wherein the
93 determination includes a recommendation for treatment.

94 31. The method as claimed in claim 30, further comprising
95 monitoring the treatment by assaying at least one vaginal sample during
96 treatment, to determine the presence or absence in the vaginal sample of
97 the one or more oxidized or carbonylated peptides.

98 32. The method as claimed in claim 30, wherein the
99 determination includes a recommendation of treatment that comprises
100 antibiotic treatment, tocolytic treatment, anti-inflammatory treatment, or
101 antioxidant treatment.

102 33. The method as claimed in claim 30, wherein the
103 determination includes a recommendation of treatment that comprises
104 inducing labor.

105 34. The method as claimed in claim 30, wherein the
106 determination includes a recommendation of treatment that comprises a
107 cesarean section.

108 35. The method as claimed in claim 22, wherein the treated
109 vaginal sample is applied to a biochip comprising an anti-dinitrophenol
110 antibody and subjected to mass spectrometric analysis that is keyed to a
111 shift in molecular weight, relative to a sample not treated with
112 dinitrophenol, that corresponds to the incorporated dinitrophenol group.

113 36. The method as claimed in claim 22, wherein the treated
114 vaginal sample is applied to a biochip comprising an anti-dinitrophenol
115 antibody and subjected to mass spectrometric analysis is keyed to a shift
116 or approximately 16 Da, relative to a sample not treated with
117 dinitrophenol, that corresponds to the molecular mass of oxygen.

118 37. The method as claimed in claim 21, wherein total carbonyl
119 content of the oxidized or carbonylated peptides is measured by
120 derivatizing the peptides with dinitrophenylhydrazine.

121 38. A method for qualifying status of the intra-amniotic
122 environment in a subject over time, comprising (i) providing spectra
123 generated by mass spectrometric analysis of at least two vaginal samples

124 taken from the subject, and (ii) extracting data from the spectra and
125 subjecting the data to pattern-recognition analysis that is keyed to at least
126 two peaks in the spectra.

127 39. A kit for detecting, from a sample of vaginal fluid, the
128 presence of at least two biomarkers indicative of status of the intra-
129 amniotic environment, comprising (a) a substrate adapted for inserting
130 into a mass spectrophotometer for analysis, and (b) instructions for
131 applying a sample of vaginal fluid to the substrate and subjecting the
132 substrate to mass spectrometric analysis.

133 40. The kit as claimed in claim 39, wherein the substrate is a
134 biochip.

135 41. The kit as claimed in claim 40, wherein the biochip
136 comprises at least one absorbent selected from a hydrophobic adsorbent
137 and a cation exchange adsorbent.

138 42. The kit as claimed in claim 40, wherein the biochip
139 comprises an anti-dinitrophenol absorbent.

140 43. The kit as claimed in claim 39, additionally comprising, in a
141 separate container, a quantity of the biomarker in pure form to be used as
142 a standard.

143 44. The kit as claimed in claim 43, a washing solution for
144 removing unbound material from the substrate.

145 45. A kit for detecting, from a sample of vaginal fluid, the
146 presence of at least one oxidized or carbonylated peptide indicative of
147 status of the intra-amniotic environment, comprising (a) a substrate that
148 binds the peptide, and (b) instructions for applying a sample of vaginal

149 fluid to the substrate and subjecting the substrate to analysis.

150 46. A kit as claimed in claim 45, comprising an ELISA substrate.

151 47. The kit as claimed in claim 45, comprising a substrate
152 adapted for insertion into a mass spectrophotometer for analysis.

153 48. The kit as claimed in claim 45, additionally comprising, in
154 separate container, a quantity of the oxidized or carbonylated peptide in
155 pure form to be used as a standard.

156 49. The kit as claimed in claim 48, a washing solution for
157 removing unbound material from the substrate.

158 50. A method for identifying biomarkers that are present in
159 vaginal fluid and are indicative of status of the intra-amniotic
160 environment, comprising:

161 (a) profiling a sample of vaginal fluid by mass
162 spectrophotometric analysis,

163 (b) profiling a sample of amniotic fluid by mass
164 spectrophotometric analysis, and

165 (c) comparing the profiles obtained in (a) and (b) to identify
166 biomarkers in vaginal fluid that also are found in amniotic fluid.

167 51. The method as claimed in claim 50, additionally comprising
168 correlating the presence or absence of the biomarkers in the vaginal fluid
169 that are also found in the amniotic fluid to a clinical status.

170 52. The method as claimed in claim 51, wherein the clinical
171 status is rupture of the fetal membrane.

172 53. The method as claimed in claim 51, wherein the clinical
173 status is intra-amniotic infection.

174 54. The method as claimed in claim 51, wherein the clinical
175 status is intra-amniotic inflammation.

176 55. A method for identifying biomarkers that are present in
177 vaginal fluid and are indicative of status of the intra-amniotic
178 environment, comprising:

- 179 (a) profiling a first sample of vaginal fluid from a subject
180 having a normal pregnancy by mass spectrophotometric analysis,
- 181 (b) profiling a second sample of vaginal fluid from a subject
182 having a pregnancy characterized by an abnormal clinical status by mass
183 spectrophotometric analysis, and
- 184 (c) correlating the presence or absence of the biomarkers in
185 the vaginal fluid to clinical status of the pregnancy.